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| APPLICATION NO.               | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.     | CONFIRMATION NO. |
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| 10/665,793                    | 09/19/2003  | Edward J. Kaplan     | KAP 100 CIP             | 6738             |
| 23579                         | 7590        | 08/30/2007           | EXAMINER                |                  |
| PATREA L. PABST               |             |                      | SAMALA, JAGADISHWAR RAO |                  |
| PABST PATENT GROUP LLP        |             |                      | ART UNIT                | PAPER NUMBER     |
| 400 COLONY SQUARE, SUITE 1200 |             |                      | 1618                    |                  |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                        |                     |
|------------------------------|------------------------|---------------------|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |
|                              | 10/665,793             | KAPLAN, EDWARD J.   |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |
|                              | Jagadishwar R. Samala  | 1618                |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) Responsive to communication(s) filed on 02 July 2007.
- 2a) This action is **FINAL**.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) Claim(s) 1-20,22-27 and 29-35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-20,22-27 and 29-35 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

|   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|   | 6) <input type="checkbox"/> Other: _____                          |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :04/03/07; 04/30/07; 09/01/06 & 07/02/07.

## **DETAILED ACTION**

### **Status of Application**

1. Acknowledgment is made of amendment filed on July 2, 2007. Upon entering the amendment, the claims 21 and 28 are cancelled and claims 1-20, 22-27 and 29-35 are amended. The pending claims 1-20, 22-27 and 29-35 and are presented for examination.

### **Information Disclosure Statement**

2. The information disclosure statement (IDS) submitted on 09/01/2006, 04/03/2007, 04/30/2007 and 07/02/2007 was noted and the submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the information disclosure statement.

Previous rejections that are not reiterated herein is withdrawn.

### **Response to Arguments**

2. Applicant's arguments filed on July 2, 2007 with respect to rejection of claims 1-14, 16-20, and 22-35 under U.S.C. 102(e) have been fully considered and are not persuasive. Applicant argues that Zamora fails to disclose an elastic strand or seed.

#### **Response:**

The instant invention relates to a method of making a brachytherapy stand or seed for implantation comprising mixing a biocompatible elastic carrier with a non-radioactive material to form an elastic brachytherapy strand or seed. And seed are

formed of a biodegradable material, which include synthetic polymers such as polyhydroxyacids (polylactic acid, polyglycolic-lactic acid) polyanydrides polyorthoesters, polyhydroxyalkanoates and the like as recited in specification (see page 9, lines 1-15). The state of art recognizes that the given polymeric materials will have certain degree of elasticity depending upon conditions of use (temperature and physiological and biological conditions, for e.g. gold is more malleable/elastic compared to iron or copper). And since, the elasticity is a relative term, the strand or seed of the instant application are not known to what extend they are flexible. Further, Zamora discloses the same biodegradable polymeric material such as poly-L-lactide, poly-D-lactide, polyglycolidepolycaprolactone, polyanhydride, polyhydroxyalkonates and thereof (see para 0049). Inherently, the bioabsorbable brachytherapy device advanced by Zamora provides strand offering reduced stiffness compared to brittle polymers with low deformability. Since the essential elements of the Zamora teaching are identical to the instant application (i.e., biodegradable polymeric material) the brachytherapy strand would form a flexible strand upon contact with organic tissue in the presence of physiological conditions and would inherently have the same physiochemical properties (such as elasticity) as set forth in the instant application.

Applicant argues that Zamora fails to include any structures in its seed to prevent migration of the seeds following implantation.

**Response:**

In response to applicant's argument that "structures in its seeds to prevent migration of the seeds", a recitation of the intended use of the claimed invention must

result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Zamora discloses brachytherapy strand have a greater density than that of tissue within which they are placed and this difference in density contributes to movement of brachytherapy device. By approximating the density of the tissue in which the device of this invention is placed, movement of the brachytherapy strand within the body is minimized (see para 0083). And further, fabrication methods and techniques permit the construction of brachytherapy devices having a variety of forms, for the delivery of localized radioactivity, and preferably also concurrent delivery of localized chemotherapeutic, bioactive or other drugs to patients for therapeutic purposes (see para 0029).

### **Claim Rejections - 35 USC § 102**

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the

international application designated the United States and was published under Article 21 (2) of such treaty in the English language.

Claims 1-14,16-20 and 22-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Zamora et al. (US 2001/0044567).

With respect to claims 1-14,16-20 and 22-35 the patent '567 discloses a brachytherapy device comprising a biocompatible biodegradable component (i.e. polymeric material), a non-radioactively therapeutic component and a biodegradable radiopaque marker (see abstract). The biodegradable component includes polymers (e.g. Poly (D,L-lactide) poly (L-lactide, (polyglycolide, poly (L-lactide-co-glycolide) that are same as those claimed (see page 2, para 0025 and page 5, para 0055). And also the biocompatible polymer such as poly(hydroxybutyrate) is included that can read as biocompatible elastic carrier to form an elastic brachytherapy seed (see page 4, para 0049) since they are essential same compounds. The size and shape of the seeds are within the scope of those claimed (see page 5, para 0057+). The non-radioactive therapeutic component includes chemotherapeutic agent such as cisplatin bleomycin, a radiosensitizer drug such as 5-halo uracil compounds (see page 7, para 0080). Zamora also teaches the radiopaque marker which includes various markers that are biodegradable such as platinum, tantalum and bismuth (see page 4, para 0051), where these markers are same as one required by claims, thus non-radionuclide imaging marker requirement is inherently met. The seeds of the device may be implanted singly, or may utilize suture strands, webs, meshes or other means to group the devices in a desired manner (see page 7, para 0085+). Methods of making the seeds are disclosed on pages 5-8, which include the steps as claimed.

Since, all the critical elements as required by instant claims are taught by the cited reference and claims are thus anticipated.

### **Response to Argument**

Applicant's arguments filed on July 2, 2007 with respect to rejection of claim 15, under U.S.C. 103(a) has been fully considered and are not persuasive. Applicant argues that Zamora or Widder fails to disclose an elastic strand or seed.

#### **Response:**

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Zamora teaches as described above (102 rejection). Widder teaches the intravascularly-administrable, magnetically localizable biodegradable carrier comprising microspheres for specific delivery/or releases of therapeutic and diagnostic agents to the desired target sites with minimum of systemic side effects. And also, Widder discloses the inclusion of magnetic particles on the surface of the microspheres to guide and localize the microspheres to the desired target sites. Thus, the microspheres taught by Widder are capable of delivering

chemotherapeutic agents to desired target site with minimum side effects and meets the limitation as recited in the instant claim.

### **Claim Rejections - 35 USC § 103**

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

Patentability shall not be negated by the manner in which the invention was made.

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zamora (US 2001/0044567) in view of Widder et al (US 4,247,406).

Claim 15 is drawn to a brachytherapy strand or seed for implantation into a subject comprising, a non-radionuclide imaging marker, and a biocompatible carrier, and further comprising an additive material such as ferromagnetic microspheres, oxygen, hemoglobin or drugs for enhancing oxygen perfusion.

Zamora discloses a brachytherapy device comprising a biocompatible biodegradable (i.e. polymeric material), a non-radioactively therapeutic component and a biodegradable radiopaque marker (see abstract).

Zamora fails to disclose the said additives (e.g. ferromagnetic micropshers).

However the inclusive of said additives into the brachytherapy strand or seeds well known in the art as shown by Widder.

Widder discloses a composition comprising microspheres formed from natural amino acid (proteins) and synthetic amino acid polymer, with magnetic particles embedded therein. The preferred polymer is human serum albumin and water soluble protein such as hemoglobin (see column 3, lines 62+).

It would have been obvious to one of ordinary skill in the art to modify the brachytherapy device form disclosed by Zamora to include microspheres formed from natural amino acid (proteins) with magnetic particles embedded as a carrier for administering water-soluble chemotherapeutic agents because Widder teaches that the incorporation of microspheres derived from natural amino acids (proteins) or hemoglobin containing magnetic particles as vehicles for site specific delivery of water-soluble chemotherapeutic agents, such as anti-cancer agents, whose use is now limited because of adverse side effects.

Because the microspheres which are formed from natural amino acids (proteins) and synthetic amino acids are biodegradable by proteolytic enzyme action, one of ordinary skill in the art would have been motivated to incorporate the microspheres formed from natural amino acid (proteins) with magnetic particles embedded therein brachytherapy seeds advanced by Zamora. Based on the teaching of Widder, there is reasonable expectation that the microspheres containing ferromagnetic particles in drug delivery system would be highly desirable for administering water-soluble

chemotherapeutic agents over extended period of time with low toxicity. As such, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate or make use of the microspheres containing ferromagnetic particles in drug delivery system advanced by Zamora in view of the Widder teaching.

### **Double Patenting**

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14, 16-20, 22-24 and 27-35 are rejected on the ground of nonstatutory obviousness type double patenting as being unpatentable over claims 1-3, 5, 10, 12, 15, 30, 32, 35 and 36 of US 6,746,661 B2. Although the conflicting claim is not identical, they are patentably distinct from each other because claim of the instant application is drawn to a brachytherapy strand or seed for implantation into a subject comprising, a non-radionuclide imaging marker, and a biocompatible carrier, wherein the strand or seed is elastic and has size and shape suitable for passing through the bore of a needle having an interior diameter of less than about 2.7 millimeters (10gauge), while the US pat. Application is a brachy therapy seed for implantation into a subject comprising one or more micropsheres, wherein each microsphere comprises at least one component selected from the group consisting of biocompatible component, a therapeutically active component and a radiopaque marker; the seed comprises a plurality of microspheres comprising a biocompatible component, one or more therapeutically active components, and a radiopaque marker; and brachytherapy seed has a size and shape suitable for passing through the bore of a needle having an interior diameter of less than about 2.7 millimeters (10 gauge). Both require brachytherapy seeds, biocompatible component, radiopaque marker and therapeutic agent. Thus, the instant claim is within the scope of

the claim of the US pat. Application. Thus scope is overlapping each other and properly included in the rejection because they are patentably distinct from each other. Thus, the claim is readily envisaged by the teaching of the prior art and the claim is properly included in the rejection.

Claims 25 and 26 are rejected on the ground of nonstatutory obviousness type double patenting as being unpatentable over claims 1-3 of US 6,514,193 B2. Although the conflicting claim is not identical, they are patentably distinct from each other 30, 32, 35 and 36 of US 6,746,661 B2. Although the conflicting claim is not identical, they are patentably distinct from each other because claim of the instant application is drawn to a brachytherapy strand or seed for implantation into a subject comprising, a non-radionuclide imaging marker, and a biocompatible carrier, wherein the strand or seed is elastic and has size and shape suitable for passing through the bore of a needle having an interior diameter of less than about 2.7 millimeters (10gauge), while the US pat. Application is a brachy therapy seed for implantation into a subject comprising one or more micropsheres, wherein each microsphere comprises at least one component selected from the group consisting of biocompatible component, a therapeutically active component and a radiopaque marker; the seed comprises a plurality of microspheres comprising a biocompatible component, one or more therapeutically active components, and a radiopaque marker; and brachytherapy seed has a size and shape suitable for passing through the bore of a needle having an interior diameter of less than about 2.7 millimeters (10 gauge). Both require brachytherapy seeds, biocompatible component, radiopaque marker and therapeutic agent. Thus, the instant claim is within the scope of

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the claim of the US pat. Application. Thus scope is overlapping each other and properly included in the rejection because they are patentably distinct from each other. Thus, the claim is readily envisaged by the teaching of the prior art and the claim is properly included in the rejection.

Claims 25 and 26 are rejected on the ground of nonstatutory obviousness type double patenting as being unpatentable over claims 1-3 of US 6,514,193 B2. Although the conflicting claim is not identical, they are patentably distinct from each other because claim of the instant application is drawn to a method for administering a therapeutically active component to a target tissue in a subject, the method comprising implanting a brachytherapy strand or seed comprising, a non-radionuclide imaging marker, and a biocompatible carrier, wherein the strand or seed is elastic, and has a size and shape suitable for passing through the bore of a needle having an interior diameter of less than about 2.7 millimeters (10 gauge), while the US Pat. Application is a method for administering a therapeutically active component to a target tissue in a subject, comprising the steps of providing a brachytherapy seed comprising a non-metal biocompatible component, a therapeutically active component comprising a non-radioactive drug, and a radiopaque marker, said biocompatible component being (a) physically associated with a therapeutically active component and (b) in contact with said radiopaque marker, wherein said brachytherapy seed has a size and shape suitable for passing through the bore of a needle having an interior diameter of less than about 2.7 millimeters (10 gauge). Both require brachytherapy seeds, biocompatible component, radiopaque marker and therapeutic agent. Thus, the instant claim is within

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the scope of the claim of the US pat. Application. Thus scope is overlapping each. other and properly included in the rejection because they are patentably distinct from each other. Thus, the claim is readily envisaged by the teaching of the prior art and the claim is properly included in the rejection.

The nonstatutory double patenting rejection is maintained and can over by filing a terminal disclaimer.

***Conclusion***

1. No claims are allowed at this time.
2. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jagadishwar R. Samala whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jagadishwar R Samala  
Examiner  
Art Unit 1618

Zohreh Fay  
Primary Examiner  
Art Unit 1618

